REMARKS

Entry of the foregoing amendments, reconsideration and reexamination of the subject application, as amended, pursuant to and consistent with 37 C.F.R. § 1.112, in light of the remarks which follow, are respectfully requested.

As correctly noted in the Office Action summary, claims 1, 3 and 4 are pending and claims 2 and 5 have been withdrawn in view of being non-elected inventions.

The amendment to the specification on page 28 rectifies a typographical error and thus does not introduce any prohibited new matter.

Claims 1, 3 and 4 have been amended. Support for the amendments can be found at least in the claims as originally filed.

New claims 6 and 7 have been added. Support for new claims 6 and 7 can be found at least at page 22, line 21 to page 23, line 19 and on page 7, lines 4-18 of the specification. The amino acid sequences presented in new claims 6 and 7 are truncations of the SEQ ID NO:1, wherein a 15 amino acid sequence has been deleted between the second and third cysteines (indicated in bold below). The sequences presented in new claims 6 and 7 lack the double-underlined 15 amino acid polypeptide from SEQ ID NO:1, which is represented below:

Lys Ala Asn Asp Phe Leu His Arg Gly Glu Tyr Ser Val **Cys** Asp
Ser Glu Glu His Trp Val Gly Asn Leu Thr Gln Ala Thr Asp Leu
Arg Gly Asn Glu Val Thr Val Leu Pro His Val Arg Ile Asn Asn
Val Val Lys Lys Gln Met Phe Tyr Glu Thr Thr **Cys** Arg Val Ser
Lys Pro Ile Gly Ala Pro Lys Pro Gly Gln Gly Val Ser Gly Val
Lys Ala Gly Thr Ser Ser **Cys** Arg Gly Ile Asp Asn Glu His Trp
Asn Ser Tyr Cys Thr Asn Val His Thr Phe Val Arg Ala Leu Thr
Ser Tyr Lys Asn Gln Ile Ala Trp Arg Phe Ile Arg Ile Asn Ala
Ala Cys Val Cys Val Leu Ser Arg Asn Ser Trp Arg His

As discussed in the specification, the 15 amino acid deletion occurs between the second and third cysteine residues (indicated in bold). Applicants assert that given the discussion of

where the insertion/deletion occurs, there is written description support for the new claims. Claims 8 and 9 are supported for the same reasons as claims 6 and 7. Thus, no prohibited new matter is entered by entry of these claims.

Applicants respectfully request an interview with the Examiner after receipt of the instant Amendment and at the convenience of the Examiner. Applicants invite the Examiner to contact the undersigned representative to discuss the application at his earliest convenience.

I. OBJECTION TO THE OATH/DECLARATION

The Oath/Declaration was objected to because a post office address was not included for each inventor. Applicants submit herewith a substitute Oath/Declaration executed by the inventors which contains the requested information. Please note that the undersigned attorney now has Associate Power of Attorney in the instant application. By this submission, the objection should be mooted and can therefore be withdrawn.

II. DOUBLE PATENTING REJECTION

Claim 4 stands objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 1. Applicants have amended claim 4, in view of the objection. Accordingly, amended claim 4 now differs from claim 1 as required by Rule § 1.75. Given the amendment, Applicants respectfully request the withdrawal of the objection under 37 C.F.R. § 1.75 and allowance of claim 4.

III. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

1. Rejection for Lack of Written Description

Claims 1, 3 and 4 stand rejected under 35 U.S.C. § 112, first paragraph, because the claims purportedly contain subject matter which is not described in the specification in such a way to reasonably convey to the skilled artisan that the inventor had possession of the claimed invention. Specifically, it is asserted that the specification solely describes carp NT-7 as depicted in SEQ ID NO:1.

Respectfully, Applicants traverse the rejection. The specification provides other variants. As discussed in the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. § 112, 1 "Written Description" Requirement, 64 Fed. Reg. 71434, "possession may be shown by actual reduction to practice". Applicants provide, for instance, an example (D15) in the specification wherein 15 amino acids are deleted between the second and third cysteines in SEQ ID NO:1. The activity of the D15 variant is discussed in Example 6 on page 23 (e.g., D15) and was described as being equivalent to the activity observed for SEQ ID NO:1. The example of D15 is an actual reduction to practice of a different NT-7 polypeptide which can be structurally envisioned.

Therefore, given the description provided in the specification and at least the above arguments, Applicants assert that there is sufficient written description in the specification to evidence possession of the claimed invention. Accordingly, Applicants respectfully request the withdrawal of the rejection under § 112, first paragraph for lack of written description.

2. Rejection for Lack of Enablement

Claims 1, 4 and 5 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Specifically, the specification is "enabling for the carp NT-7 polypeptide of SEQ ID NO:1, or functional variants thereof that increase survival and neurite outgrowth of embryonic chick DRG neurons". However, the specification is purportedly not enabling "for NT-7 polypeptides with no recited structural nor functionally [*sic*] characteristics, nor any biologically functional equivalents of such without specific structural and functional characteristics."

Applicants note that claim 5 has been withdrawn from consideration because it is directed to non-elected subject matter. Turning to the rejection of claims 1 and 4 for lack of enablement, Applicants traverse the rejection. Respectfully, Applicants provide guidance as to the minimal structural requirements necessary for any NT-7 polypeptide to function. For example, Applicants constructed a truncated form of NT-7 that lacked the

15-amino acid insertion, NT-7 (D15) (see page 22). The D15 polypeptide was shown to have comparable activity to that observed for SEQ ID NO:1 (as discussed in Example 6, page 23). Additionally, the six cysteine residues are conserved among the various neurotrophins (page 19, lines 10-12); these are highlighted below:

Lys Ala Asn Asp Phe Leu His Arg Gly Glu Tyr Ser Val **Cys** Asp
Ser Glu Glu His Trp Val Gly Asn Leu Thr Gln Ala Thr Asp Leu
Arg Gly Asn Glu Val Thr Val Leu Pro His Val Arg Ile Asn Asn
Val Val Lys Lys Gln Met Phe Tyr Glu Thr Thr **Cys** Arg Val Ser
Lys Pro Ile Gly Ala Pro Lys Pro Gly Gln Gly Val Ser Gly Val
Lys Ala Gly Thr Ser Ser **Cys** Arg Gly Ile Asp Asn Glu His Trp
Asn Ser Tyr **Cys** Thr Asn Val His Thr Phe Val Arg Ala Leu Thr
Ser Tyr Lys Asn Gln Ile Ala Trp Arg Phe Ile Arg Ile Asn Ala
Ala **Cys** Val **Cys** Val Leu Ser Arg Asn Ser Trp Arg His

Applicants also note that discussion is provided in the Examples of how variants can be routinely screened for activity, as was done for D15 and SEQ ID NO:1. Thus, for at least these reasons, Applicants provide in the specification sufficient description by which the skilled artisan would know how to make and use the invention. According, in view of at least the above arguments, Applicants request the appropriate withdrawal of the rejection under § 112, first paragraph and allowance of the claims.

IV. REJECTION UNDER 35 U.S.C. § 102(A)

1. Lai *et al.*

Claims 1, 3 and 4 stand rejected under § 102(a) as anticipated by Lai *et al.* (Molecular and Cellular Neuroscience 11: 64-76, 1998). Lai *et al.* is cited for teaching "isolation of a carp NT-7 polypeptide that is 100% to SEQ ID NO.1".

Applicants traverse the rejection. Applicants submit that the reference by Lai *et al.* represents Applicants' own work. Applicants submit with this response two Declarations under 37 C.F.R. § 1.132, executed by each inventor, Kwok On Lai and Nancy Yuk-Yu Ip. The Declarations evidences that the inventorship of the application is correct, notwithstanding the authorship of the article, as required by M.P.E.P. § 716.10 and *In re* Katz, 687, F.2d 450, 455 (C.C.P.A. 1982).

Drs. Lai and Ip are co-authors of the above-identified reference, as well as named inventors on the instant application. The remaining authors, Wing-Yu Fu and Fanny C. F. Ip, are not inventors. These two authors are listed on the publication because they performed work under the direction and at the behest of Dr. Nancy Ip. These individuals did not contribute to the conception of the invention and therefore cannot be considered as inventors. Given the above arguments and the attached Declarations under 37 C.F.R. § 1.132, Applicants submit that the rejection has been obviated. Accordingly, Applicants respectfully request that the rejection of claims 1, 3 and 4 under 35 U.S.C. § 102(a) be withdrawn and the claims allowed.

2. Nilsson et al.

Claims 1, 3 and 4 stand rejected under § 102(a) as anticipated by Nilsson *et al.* (FEBS Letters 424: 285-290, March 13, 1998). Nilsson *et al.* was cited for purportedly teaching the isolation of a NT-7 polypeptide from zebrafish that is 92% identical to SEQ ID NO:1 and disclosing fragments thereof.

Applicants traverse the rejection. The article by Nilsson *et al.* was published March 13, 1998. Submitted with this Amendment and Reply is a Declaration of Dr. Nancy Yuk-Yu Ip under 37 C.F.R. § 1.131. In this Declaration under § 1.131, Dr. Ip asserts that the

claimed subject matter was invented prior to the effective date (March 13, 2001) of the reference relied upon in the rejection. Applicants assert that the claimed subject matter was invented at least by January 8, 1998. The date of January 8, 1998 is when the manuscript, which describes the inventive subject matter, was accepted for publication by the editorial board of Molecular and Cellular Neuroscience. The accepted manuscript is substantial the same, except for format, to the article by Lai *et al.* as it appears in Molecular and Cellular Neuroscience. The acceptance date is reflected on page 76 of the Exhibit A (Kwok On Lai *et al.*, Molecular and Cellular Neuroscience 11: 64-76, 1998).

In view of the attached Declaration, Exhibit and above arguments, Applicants respectfully submit that the rejection is obviated and should appropriately be withdrawn. Accordingly, Applicants request allowance of the claims.

CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,

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Date: April 6, 2001

Attachment to Amendment and Reply dated April 6, 2001

Marked-up Copy

Page 28, Paragraph Beginning at Line 11

One important feature of NT-7 is the insertion of 15 amino acids at the position corresponding to the insertion of *Xiphophorus* NT-6. The insertion lacks the GT-AG sequence that is conserved in the intron/exon boundary. This, together with the result of RT-PCR, suggested that the insertion did not represent an intron. Since the activity of NT-7(D15) was as potent as NT-7 in both the DRG assay and the phosphorylation assay, the 15-amino-acid insertion was not indispensable in its biological activity. Its presence in the NT-7 molecule might be accessory to its neurotrophic function, such as binding to extracellular matrix which helped to localise the [facator] factor in the target area. If that is the case, it will be interesting to examine whether NT-7, like NT-6, binds to heparan sulfate or other types of molecules present in the extracellular matrix.

Attachment to Amendment and Reply dated April 6, 2001

Marked-up Claims 1, 3 and 4

1. (Amended) An essentially purified neurotrophin[, NT-7] of carp, carp NT-7 having neurotrophic activity and an amino acid sequence [SEQ ID NO.: 1] as follows:

Lys Ala Asn Asp Phe Leu His Arg Gly Glu Tyr Ser Val Cys Asp
Ser Glu Glu His Trp Val Gly Asn Leu Thr Gln Ala Thr Asp Leu
Arg Gly Asn Glu Val Thr Val Leu Pro His Val Arg Ile Asn Asn
Val Val Lys Lys Gln Met Phe Tyr Glu Thr Thr Cys Arg Val Ser
Lys Pro Ile Gly Ala Pro Lys Pro Gly Gln Gly Val Ser Gly Val
Lys Ala Gly Thr Ser Ser Cys Arg Gly Ile Asp Asn Glu His Trp
Asn Ser Tyr Cys Thr Asn Val His Thr Phe Val Arg Ala Leu Thr
Ser Tyr Lys Asn Gln Ile Ala Trp Arg Phe Ile Arg Ile Asn Ala
Ala Cys Val Cys Val Leu Ser Arg Asn Ser Trp Arg His

or functional variants, analogues and functional fragments of NT-7.

3. (Amended) A composition comprising an essentially purified neurotrophin[, NT-7] of carp, carp NT-7 having neurotrophic activity and an amino acid sequence [SEQ ID NO.: 1] as follows:

Lys Ala Asn Asp Phe Leu His Arg Gly Glu Tyr Ser Val Cys Asp
Ser Glu Glu His Trp Val Gly Asn Leu Thr Gln Ala Thr Asp Leu
Arg Gly Asn Glu Val Thr Val Leu Pro His Val Arg Ile Asn Asn
Val Val Lys Lys Gln Met Phe Tyr Glu Thr Thr Cys Arg Val Ser

Attachment to Amendment and Reply dated April 6, 2001

Marked-up Claims 1, 3 and 4

Lys Pro Ile Gly Ala Pro Lys Pro Gly Gln Gly Val Ser Gly Val
Lys Ala Gly Thr Ser Ser Cys Arg Gly Ile Asp Asn Glu His Trp
Asn Ser Tyr Cys Thr Asn Val His Thr Phe Val Arg Ala Leu Thr
Ser Tyr Lys Asn Gln Ile Ala Trp Arg Phe Ile Arg Ile Asn Ala
Ala Cys Val Cys Val Leu Ser Arg Asn Ser Trp Arg His

or functional variants, analogues and functional fragments of NT-7.

4. (Twice Amended) [An] A method of treating acute and/or chronic neuronal injury or degenerative states for a specific subclass of neurons, comprising administering to a subject an essentially purified neurotrophin of carp, carp NT-7 of claim 1 [having neurotrophic activity and an amino acid sequence [SEQ ID NO.: 1] as follows:

Lys Ala Asn Asp Phe Leu His Arg Gly Glu Tyr Ser Val Cys Asp
Ser Glu Glu His Trp Val Gly Asn Leu Thr Gln Ala Thr Asp Leu
Arg Gly Asn Glu Val Thr Val Leu Pro His Val Arg Ile Asn Asn
Val Val Lys Lys Gln Met Phe Tyr Glu Thr Thr Cys Arg Val Ser
Lys Pro Ile Gly Ala Pro Lys Pro Gly Gln Gly Val Ser Gly Val
Lys Ala Gly Thr Ser Ser Cys Arg Gly Ile Asp Asn Glu His Trp
Asn Ser Tyr Cys Thr Asn Val His Thr Phe Val Arg Ala Leu Thr
Ser Tyr Lys Asn Gln Ile Ala Trp Arg Phe Ile Arg Ile Asn Ala
Ala Cys Val Cys Val Leu Ser Arg Asn Ser Trp Arg His

Attachment to Amendment and Reply dated April 6, 2001

Marked-up Claims 1, 3 and 4

or functional variants, analogues and functional fragments of NT-7 in the treatment of acute and/or chronic neuronal injury or degenerative states for a specific subclass of neurons].